

# Mesoionic Compounds and Its Structural Overview: A Theory

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## INTRODUCTION

Compounds that are currently grouped together under the heading of mesoionic have been recognized for longer than a century. Since that time, numerous developments and modifications have been made, not only to the concept of mesoionic compounds, but also to the procedures that are utilized to manufacture them. Definitions of mesoionic compounds that are broadly analogous were proposed by Quis, Ramsden, and Potts in response to an important essay written by Schonberg, Baker, and Ollis. They either said outright or strongly indicated that they have a fragrance quality. These definitions should be used in conjunction with Structure.

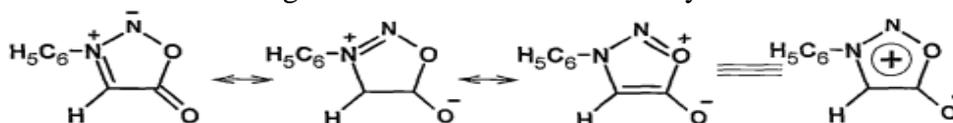
### AUTHOR'S WORD

According to Miller, Simas, and others research, mesoionic compounds are not aromatic despite the fact that they are firmly stabilized by 7c-electron and charge delocalization. They came up with the following definition for mesoionic compounds: "Mesoionic compounds are planar five-membered heterocyclic betaines. They have at least one side chain whose a-atom is also in the ring plane. Their dipole moments are on the order of 5D." The electrons are dispersed throughout two distinct regions that are linked together by a single covalent bond. The a-atom that makes up the side chain can be found in both the HOMO and the LUMO regions. The HOMO region is associated with the negative 7i-charge, and the LUMO region is associated with the positive 7i-charge. This description provides information regarding structure. It is important to keep in mind that the values C, N, O, S, or Se are assigned to the letters a, b, c, d, e, and f on a regular basis.



### Mesoionic heterocycles are represented

Baker and Ollis first introduced the term "mesoionic" (mesomeric + ionic) in 1949 to refer to the structure of H-phenylsydnone as a resonance hybrid of the dipolar resonating structures. This was done in order to distinguish it from other resonance hybrids of the time.



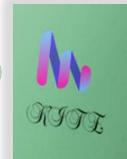
### N-phenylsydnone's resonant structure

## MEMBERS OF MESOIONIC

In its earliest iteration, the term "mesoionic" referred to "a five- or six-membered heterocycle that cannot be satisfactorily represented by any one covalent or polar structure and possesses a sextet of electrons in association with the atoms comprising the heterocyclic ring." However, the definition of mesoionic heterocycle has evolved, and the term is now exclusively used to refer to five-membered heterocycles. Previously, the term could refer to any heterocycle with more than five members.

a five-membered heterocycle that cannot be accurately represented by a single covalent or polar structure due to the fact that it possesses a sextet of electrons that are bonded to the five atoms that make up the ring.

The overarching structure of the mesoionic heterocycles can be described in the following way: where a, b, c, d, e, and f are carbon-derived or hetero-derived atoms or groups of atoms. A comparable fractional negative charge on an exocyclic atom or set of exocyclic atoms that



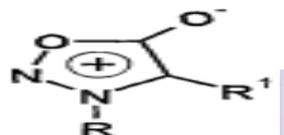
is covalently bonded to the ring through a carbon atom cancels out the fractional positive charge that is present on the heterocyclic atoms.

An exocyclic heteroatom is covalently bonded to the heterocyclic ring known as a betain through a cyclic heteroatom rather than through the carbon atom. Betains are five-membered heterocycles. Betains make up a subset of the mesoionic chemical family. The details are illustrated as in and include several N-oxides and N-imides.

### CRITERIA OF CATEGORIZATION

In order for a molecule to be categorized as mesoionic, it needs to satisfy the following criteria: (1) it needs to have a fully delocalized positive and negative charge; (2) it needs to be planar; it needs to contain a five-membered heterocyclic ring with an exocyclic atom or group that is capable of bearing a significant amount of negative charge density; and (3) it needs to have a significant resonance energy. In 1953, Baker and Ouis formally established these conditions in their document. Because of these three characteristics, it was feasible to distinguish mesoionic systems from zwitterions that are closely linked to them, such as betaines, ylides, and zwitterions. The latter species have some degree of charge fixing, in contrast to the mesoionic systems, which have charges that are dispersed throughout the system.

At the moment, the 'mesoionic' structure of sydnone that was proposed by Baker and Ouis is probably the one that is used the most frequently.



In the field of medicinal chemistry, mesoionic compounds, also known as heterocyclic betaines, are particularly beneficial due to their wide range of well-established pharmacological activities as well as their low level of toxicity. It is especially noteworthy that their anticancer activity can be attributed to exceedingly favorable in vivo results. Research that has been conducted on the chemistry of mesoionic rings, namely their use as concealed dipoles, has produced beneficial results since the late 1950s.

The symbol is used to indicate electronic distributions of mesoionic compounds.

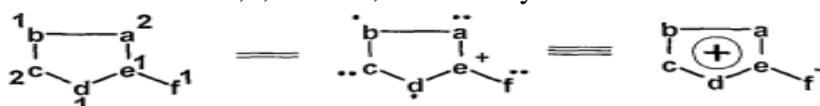
### The Classification of Mesoionic Heterocycles;

It is possible to differentiate between type-A and type-B mesoionic heterocycles by looking at the number of electrons contributed by the ring atoms to the ring's π-electron system.

#### (I) Type-A:

The illustration to the right depicts a type-A mesoionic heterocycle, which is distinguished by the fact that the two atoms of the five-membered ring that are not next to one another each contribute two electrons to the π-electron system.

If the letters a, b, c, d, e, and f are correctly swapped for carbon and hetero atoms (nitrogen, oxygen, and sulfur), then the general structural formula for type-A mesoionic heterocycles can produce 144 different possible structures. These structures are referred to as the structural possibilities. However, there have only been about 70 of these type-A mesoionic heterocycles documented, such as 1,2,3-oxadiazolium-5-olate (Sydnone), 1,3,4-thia-1,4-dicarboxylate, and 1,3,4-thia-1,4-dicarboxylate.



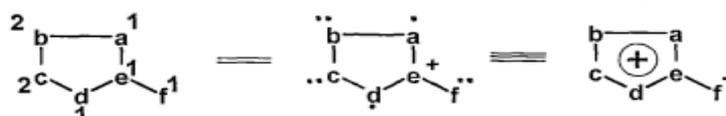
Type-A mesoionic heterocycles are shown as having a and c each contributing two electrons, while b, d, e, and f each adding one electron to the π electron system.

#### (II) Type-B:

The mesoionic heterocycles classified as type-B and illustrated in the following way are the ones in which each of two adjacent atoms of the five-membered rings contributes two electrons to the π-electron system.



In the standard structural representation of mesoionic heterocycles of type B, the letters a, b, c, d, e, and f stand for groups produced from the carbon and hetero atoms (N, O and S). While groups a, d, e, and f each contribute one electron to the 7i-electron system, groups b and c each contribute two electrons to the system. There are 84 possible configurations when considering this structural type; nevertheless, approximately 15 mesoionic heterocycles of type-B have been found up to this point as an illustration. 1,2-dithiolium-4-olate, 1,2,3,4-tetrazolium-5-thiolate, etc. 1,2-diazolium-4-aminide is another example.



A representation of type-B mesoionic heterocycles, in which b and c each provide 2  $\pi$ -electrons, and a, d, e, and f each contribute 1  $\pi$ -electron to the structure. The two types of mesoionic heterocycles display quite different chemical properties, and they are as follows: Because these heterocycles are considered to be produced from the union of 1,3-dipoles and heterocumulenes, they are able to take part in 1,3-dipolar cycloaddition events. Type-A mesoionic heterocycles participate in these reactions..



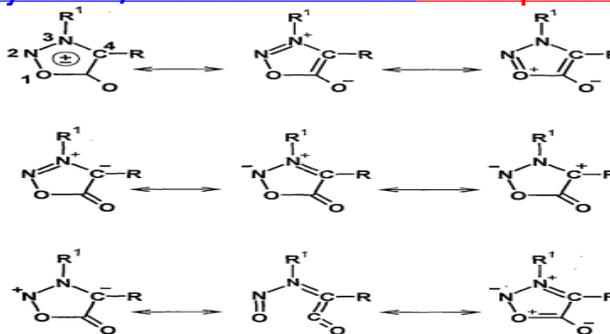
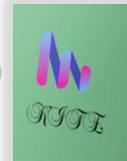
One of the chemical properties of type-B mesoionic heterocycles is their capacity to quickly open their rings and create acyclic valence tautomers.



The sydnone ring is the only mesoionic compound that is known to undergo a vast range of chemical reactions that are helpful for synthetic reasons. As a result, it is the mesoionic compound that has been the subject of the greatest amount of research out of all of the mesoionic compounds. It is simple to produce using primary amines as the starting material. In 1935, researchers at the University of Sydney in Sydney, Australia, developed the very first sydnone. According to Earl and Mackney, a treatment with acetic anhydride on A-nitroso-A'-phenylglycine yielded a neutral, anhydro derivative. It was this anhydro derivative that the bicyclic structure was attributed to. As a result of the reaction's wide range of applications, a number of compounds with similar properties were synthesized and given the name "sydnone" (as a nod to the fact that they were developed in Sydney, Australia). The name Sydney was created by taking the initials of the word lactone and rearranging them to get the first four letters of the name. SYDNOne can be created by adding lactONE to SYDNey.



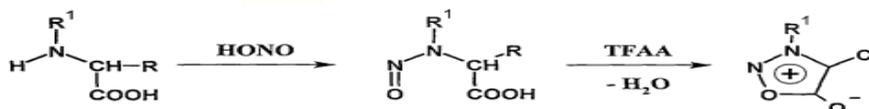
As the chemical and physical properties of the sydnones were explored in greater depth, it became evident that the structure was in fact erroneous. In contrast to the stretched, bicyclic portrayal, sydnones provide signs of higher degrees of polarity, stability during heating, and less reactivity toward acids and bases. These characteristics are all positive. As a consequence of this, Baker, Ollis, and Poole arrived at the conclusion that sydnones were monocyclic, dipolar derivatives of oxadiazolone in the 1940s. They published a number of studies to support their findings and are credited with establishing this theory. The structure is the chosen representation for the multiple possible resonance hybrids because it enables a wide variety of canonical representations.



Because of the unique characteristics of the sydnone ring system, Baker, Ollis, and Poole suggested that sydnones should be placed in their own distinct class that they dubbed "mesoionic" (also written as "mesomeric/ionic"). Up until the official requirements for a molecule to be classed as mesoionic were put down in IQSS, they continued to express the fundamental notions that underpinned their electrical structure. After that, the following characteristics were proposed as necessary for a molecule to be considered mesoionic:

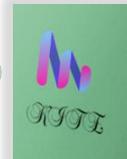
- (1) Possess both a positive and a negative charge that is distributed evenly across the object.
- (2) Possess a five-membered heterocyclic ring that is planar and possesses an exocyclic atom or group that has the potential to support a considerable quantity of negative charge density.
- (3) Possess a significant amount of resonance energy.

Because of these three characteristics, it was feasible to distinguish mesoionic systems from dipolar entities that were nominally connected to them, such as ylides and zwitterions. The later species demonstrates strong charge localization, in contrast to the mesoionic systems, which have a charge distribution that is delocalized and cannot derive a single resonant form. The cyclodehydration of an N-nitroso- $\alpha$ -amino acid that has been  $\beta$ -substituted has remained the only standard method for obtaining sydnones ever since their first manufacture in 1935. This process has been in use ever since. R can be hydrogen, an aryl, or an alkyl substituent; however, R1 must be either an aryl or an alkyl because hydrogen produces prototropy, which results in a neutral species. R can be any of these three things. In order to create 7V-nitroso amino acid, a TV-substituted glycine is commonly nitrosated with nitrous acid. This strategy has not been successful in creating sydnones with acid-sensitive functional groups since the nitrosation phase requires the use of very acidic reaction conditions. Consequently, this strategy has not been used. This conventional method, on the other hand, has been altered to make use of dimethoxyethane and isoamyl nitrite in order to accomplish nitrosation under conditions that are not acidic. Because of this, some varieties of sydnone that were previously unable of being manufactured can now be manufactured with a yield that ranges from satisfactory to excellent.



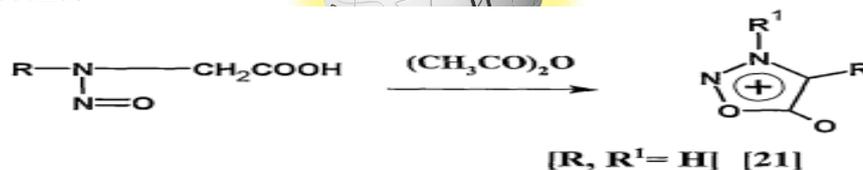
During the first stages of the cyclodehydration process, Earl and Mackney worked with acetic anhydride at room temperature for a period of six days. Since then, several treatments utilizing phosphorus pentoxide, trifluoroacetic anhydride (TFAA), heating in acetic anhydride or thionyl chloride, and heating in acetic anhydride have all been demonstrated to be beneficial enhancements. It is now the method of choice since the reaction with TFAA may frequently take place in a short amount of time (just fifteen minutes), at a low temperature (five degrees Celsius to zero degrees Celsius), and in high yields (more than ninety percent for 7V-phenylsydnone). When compared to the cost of other reagents, this reagent's price tag is substantially lower; this is the sole drawback to using it.

The cyclization described above has been performed by the utilization of more cutting-edge synthetic methods. The following types of applications are included here:



- (1) The reaction of acetic anhydride with ultrasonication at room temperature,
- (2) The halide of sodium,
- (3) The substance designated by the chemical formula N, iV-dimethylchloro-sulfitemethanium chloride
- (4) The 2-chloro-3-dimethylimidazolium chloride.

Although these novel procedures are exciting, it is unlikely that they will ever be able to take the place of the TFAA cyclization process because of its speed, effectiveness, and reusability. Compounds containing a 1,2,3-oxadiazole nucleus were the first members of this family to be discovered; we call the substances containing this nucleus sydnones. The reaction of acetic anhydride with the N-substituted a-nitroso derivatives of amino acids results in the formation of these compounds.



The sydnones are a derivative of the 1,2,3-oxadiazole family. The chemical compound sydnone has been given the name 1,2,3-oxadiazolium-5-olates by the IUPAC. Recent research efforts have been concentrated on oxydiazoles and their derivatives, which are significant members of a class of heterocyclic compounds known as oxydiazoles. Numerous studies have been written about their chemistry as well as their application. Compounds based on oxadiazole have been associated with a wide range of biological activities, some of which include antituberculostatic, antiinflammatory, analgesic, antipyretic, and anticonvulsant properties.

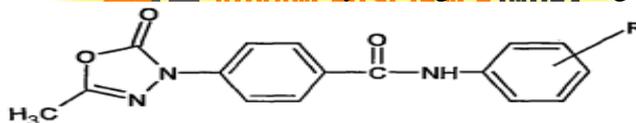
Oxydiazole derivatives are the Electron Conducting and Hole Blocking (ECHB) components that are utilized in organic Light Emitting Diodes the majority of the time. High electron transport characteristics are exhibited by the electron-deficient oxadiazole ring, however low hole transport characteristics are demonstrated.

Both R. R. Kamble and B. S. Sudha were successful in the production of 1,3,4-oxadiazole derivatives when they used sydnone.

S. G. Mallur and B. V. Badami developed a method in which 3-arylsydnones may be converted into 3-aryl-5-methyl-1,3,4-oxadiazolin-2-ones by a single procedure using bromine in acetic anhydride. Antibacterial activity of the 3-aryl-5-methyl 1,3,4-oxadiazolin-2-one derivatives has been shown to be equivalent to that of regularly used medications.

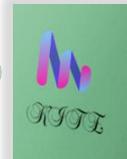
## LITERATURE REVIEW

P. Latthe and B. V. Badami were successful in the production of N-aryl-4-(5-methyl-[1,3,4]-oxadiazoline-2-one-yl) substituted benzemides because they used a process known as a one-pot ring conversion to convert 3-(4-carboxy)phenyl sydnone into 1,3,4-oxadiazolin-2-one. When compared to the standard treatment, many of these compounds demonstrated significantly higher levels of antibacterial activity during the screening process.



The molecule known as sydnone is a mesoionic compound that has an aromatic heterocycle that is not benzenoid. The fractional positive charge that is found on the sydnone ring is cancelled out by the presence of a covalently connected oxygen that carries a comparable negative charge. Because of its unusual molecular structure, sydnone possesses a conjugated character as well as a polar character, which enables it to be sensitive to magnetic as well as electric fields.

Sydnone is a one-of-a-kind compound that possesses features that are distinctively mesoionic. It would appear that the reactivity and stability of compounds containing sydnone are relatively distinct from those of other aromatic compounds. Sydnones are examples of



dipolar pseudo-aromatic heterocycles. All the way around the ring, the electron density fluctuates in a manner that is easily distinguishable. Because of these properties, there has been extensive research conducted into the chemical, physical, and biological properties of sydnones, as well as the potential applications for these compounds.

A lot of attention has been focused on the chemical and physical properties of sydnone and its derivatives because of the distinctive electronic structure and physical characteristics that both of these properties possess. Differences in the number of electrons that are contained within N(3) and C(4) are responsible for their distinct properties. There is a possibility of both positive and negative charge distributions, however this is contingent on the resonant properties of the sydnone rings. N(3) possesses a positive charge and an electron-withdrawing group, whereas C(4) has a greater number of electrons and functions as an electron donor. These findings are based on the chemical properties and computations.

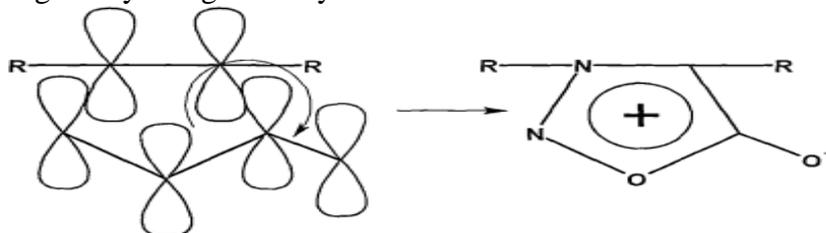
Sydnone is a chemical that belongs to the heterocyclic aromatic group but is not benzenoid. At the fourth position of the sydnone ring, several of the most fundamental aromatic processes take place. These reactions include halogenation, nitration, acylation, and sulfonation. Other functional groups such as phosphino, silyl, alkyls, halides, and so on can also functionalize these processes.

### DIPOLE CYCLOADDITION REACTION

The use of sydnones as precursors to hydrazines, as 1,3-dipoles in cycloaddition reactions, as electrolytic solvents for non-aqueous batteries, and as catalysts for the creation of micelles during molecular aggregation are all important chemical reactions. Sydnones can also be used as electrolytic solvents for non-aqueous batteries. Because of their capacity to form liquid crystals, certain sydnones have also been included into azo dyestuffs. This is done for the same reason.

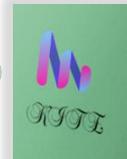
In general, alkyl sydnones are more toxic than aryl sydnone, which is also more active in its chemical reactions. In addition to their use as antibacterial agents, chalcone analogs are also widely studied. Sydnones are polar compounds that are chemically inert. They have a high degree of stability.

The fragrant quality of the ring can be traced back to the ancient sextet concept. The five atoms that make up the ring, each of which has one 2pz electron located on the exocyclic atom, are responsible for the contribution of a total of seven 2pz electrons. A sextet of electrons is created whenever one of the seven electrons in 2pz mates with the solitary electron in an exocyclic atom. The circle represents the six electrons that went through delocalization and were found to be ring currents through the use of H NMR spectroscopy. This charge polarization can be demonstrated by the huge dipole moments (4-6D) that are possessed by the mesoionic rings. The positively charged ring will be neutralized by the presence of the negatively charged exocyclic atom.

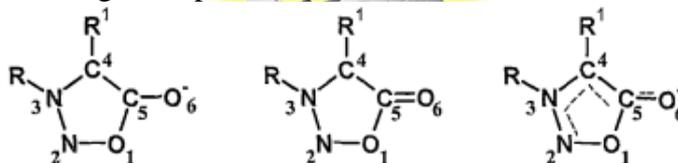


### P-orbital overlap in the sydnone ring

It is believed that the aromatic quality of the ring system is caused by its arrangement, which results in a separation of charges on a net basis. Crystalline solids make up the vast majority of arylsydnone compounds. Due to the fact that alkylsydnones are either liquids or solids with a low melting point, they can frequently be distilled in vacuum without appreciably breaking down. The petroleum ether and hexanes are two examples of nonpolar solvents that represent significant deviations from this norm. There is a large variety of organic solvents in which sydnones can be dissolved. In addition, sydnones frequently do not dissolve in water



unless a polar functional group is included in the chemical composition of the compound first. Another role that sydnones play in the body is that of free radical scavengers. Sydnones are typically described as being fragrant due to the fact that they possess this property. According to an analysis of the X-ray structures of these compounds, the exocyclic C-O link is in fact a double bond. This was discovered through the analysis. As a direct consequence of this, the resonance structure is, to put it politely, misleading. It is impossible for any model to account for the experimental observations, such as the ester-like single bond character of C5-O1 (1.41 Å) or the unequal delocalization of the sydnone ring. The NMR and X-ray diffraction findings also point to the same conclusion.



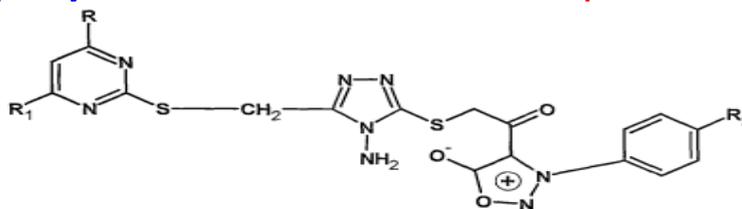
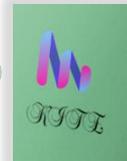
Before recommending the semi aromatic structure, Neplek and his colleagues carried out a comprehensive theoretical examination of a variety of sydnone derivatives. They looked at the projected bond ordering as well as the experimental bond lengths.

The use of sydnones as synthons has become commonplace in the field of organic synthesis, and their contributions to the advancement of heterocyclic chemistry theory have been substantial. The photochromic properties of a sydnone were found for the first time thanks to the work of Tien and Hunsberger. Some of the sydnone derivatives changed color when they were put in the presence of Ught. The hue of sydnone halogen derivatives can be permanently altered by exposure to ultraviolet radiation. Chemicals known as sydnones are classified as mesoionic compounds because of their planar, five-membered, heterocyclic betain structures that have dipole moments of around 6D. In order to investigate the electrical structure of sydnones, both semi-empirical and ab initio methods of analysis have been utilized. Even while ab initio techniques might be able to anticipate their geometry, the calculated charge distributions do not match the results of the experiments.

Using iV-acyl residues that contain mesoionicheterocycUc groups, a great number of variants of the cephalosporin and penicillin kinds have been developed; the general structures of each of these types are as follows, respectively. Others have shown that they possess a variety of antibacterial effects, in addition to in vivo antistreptococcal and antistaphylococcal activity. An important antitumor activity of SYD-1 (3-[4-chloro-3-nitro phenyl]-1,2,3-oxadiazolium-5-olate) was demonstrated by Halila and her colleagues. An investigation of the influence of the mesoionic substance sydnone SYD-1 on the energy-related functions of rat liver mitochondria. Their findings indicate that SYD-1 reduces the efficiency of oxidative phosphorylation and electron transport, which leads them to hypothesize that these effects may play a role in the antitumor activity of the compound.

## DISCUSSION

B. Kalluraya et al synthesized a series of 4-[5-(4,6-disubstituted-2-thiomethylpyrimidyl)-4'-amino-1,2,4-triazol-3'-yl]thioacetyl-3-aryl sydnones by the reaction of 5-(4,6-disubstituted-2-thiomethylpyrimidyl)-4-amino-3-mercapto-1,2,4-triazoles with 3-aryl-4-bromoacetyl sydnones in an ethanol medium. The newly synthesized compounds were tested for their antibacterial activity against E. coli and S. marcesens as well as A. niger and Pencillium. The results of these tests were positive. At a concentration of 10 ig/mL, the majority of the compounds that were evaluated demonstrated considerable antifungal activity, particularly against Pencillium. This activity was comparable to that of the conventional medication flukanazole.

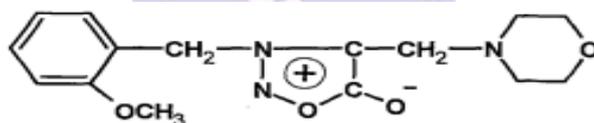


The antioxidant activity of sydnonyl substituted thiazolidinone and thiazoline derivatives has been produced by M. H. Shih and F. Y. Ke, and the results have been assessed.<sup>^^</sup> They have synthesized 3-aryl-4-formylsydnone, 4'-phenyl thiosemicarbazones and 3-aryl-4-formylsydnone 4'-thiosemicarbazones, which are precursors of 3-aryl-4-heterocyclic sydnone, are prepared by the condensation of 3-aryl-4-formylsydnone with 4'-phenylthiosemicarbazides and thiosemicarbazide, respectively. Producing heterocyclic substituted sydnone derivatives with 4-oxo-thiazolidine and thiazoline groups requires the thiosemicarbazone to react with **Wikipedia** reagents such as ethylchloroacetate and 2-bromoacetophenone. It was determined whether the chemicals that were produced had any antioxidant activity. Some of these compounds have powerful DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging action, which is comparable to that of vitamin E. Other compounds in this group do not possess this activity.

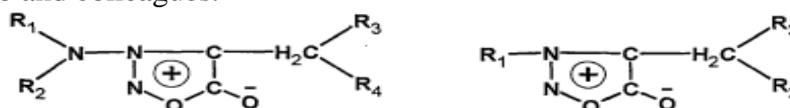
Because the Mannich reaction with mesoionic compounds, particularly with sydnone, has been the subject of a significant number of research articles and patents, secondary amine is the type of amine that is most commonly used for the reaction.

In the field of organic chemistry, the Mannich reaction is considered to be one of the most important preparative C-C bond formation reactions. The pharmacological effects of mannich bases are quite powerful and include antibacterial, antifungal, antiviral, antimalarial, anticonvulsant, and central nervous system (CNS) depressive properties.

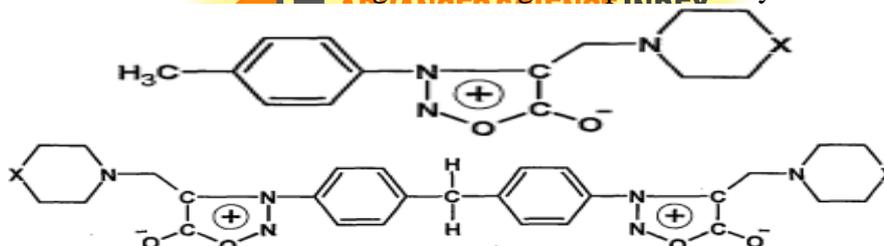
The compound known as 3-(o-methoxybenzyl)-4-morpholino methyl sydnone was manufactured by Hesin-Ju Tien, Yan-Hong Tsai, Wen-Yuan Yeh, Jong-Chang Yeh, and Yaw-Kuen Lee.



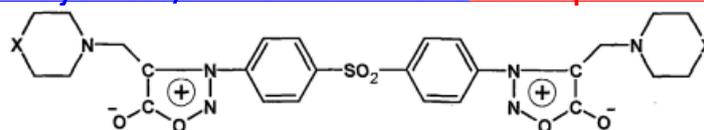
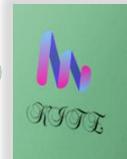
Novel analgesic sydnone derivatives with the following formula have been developed by Yoshio Imashiro and colleagues.



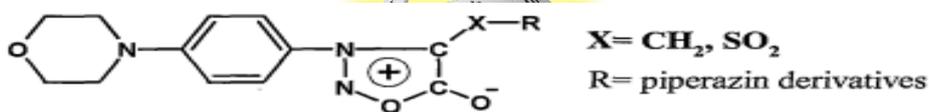
K. C. Patel and Others The antibacterial, antifungal, anticancer, and antiviral properties of a number of mono and bis(V-Mannich bases including 3-(4-methylphenyl)-4-(substituted-1/4-ylmethyl) sydnone scaffolds were investigated through the process of synthesis.



After starting with 4,4'-diaminodiphenylsulfone, K. C. Patel and his colleagues were able to produce 3,3'-(sulfonyldi-1,4-phenylene)bis4-[(substituted-1-yl)methyl]sydnone. all of the synthetic substances that were tested to see if they had any antibacterial properties.



K. C. Patel and colleagues fabricated it. Derivatives of sydnone such as 3-[4-(morpholin-4-yl)phenyl]As starting material, -4-(secondary substituted amino-4-yl methyl/ sulfonyl)-sydnone and 4-chloroaniline were utilized. The resulting compounds were examined to see whether or not they possessed any antibacterial properties. There are some excellent antibacterial drugs among them.



According to the research that was conducted, the antibacterial activity of bis-heterocyclic compounds was significantly higher than that of heterocyclic compounds. Our research is focused on the search for new powerful antibacterial compounds. In this paper, we report the synthesis and characterisation of sydnones sulfonamide and methylene derivatives substituted with benzothiazole and benzimidazole heterocycles. These derivatives were substituted with benzothiazole and benzimidazole.

## References

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